Summary Minutes of the Drug Safety and Risk Management Advisory Committee Meeting

January 24-25, 2013

Location: FDA White Oak Campus, Building 31, the Great Room, White Oak Conference Center (Rm. 1503), Silver Spring, MD

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

These summary minutes for the January 24-25, 2013 Meeting of the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration were approved on 3/13/13 I certify that I attended the January 24-25, 2013 Meeting of the Drug Safety and Risk Management Advisory Committee and that these minutes accurately reflect what transpired.	
Nicole Vesely, PharmD	James H. Woods, PhD
Acting Designated Federal Officer	Acting Chairperson
Drug Safety and Risk Management	•
Advisory Committee	

for

Kristina Toliver, PharmD Designated Federal Officer Drug Safety and Risk Management Advisory Committee The Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on January 24-25, 2013 at the FDA White Oak Campus, Great Room (Rm. 1503), White Oak Conference Center (Room 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, members and temporary voting members were provided copies of the background material from the FDA and the Generic Pharmaceutical Association. The meeting was called to order by James H. Woods, PhD (Acting Chairperson); the conflict of interest statement was read into the record by Kristina A. Toliver, PharmD (Designated Federal Officer). There were approximately 125 persons in attendance. There were 21 Open Public Hearing speakers.

Issue: On January 24 and 25, 2013, the committee met to discuss the public health benefits and risks, including the potential for abuse, of drugs containing hydrocodone either combined with other analgesics or as an antitussive. The Department of Health and Human Services received a request from the Drug Enforcement Administration for a scientific and medical evaluation and scheduling recommendation for these products in response to continued reports of misuse, abuse, and addiction related to these products. The committee also discussed the impact of rescheduling these hydrocodone products from Schedule III to Schedule II.

Attendance:

Drug Safety and Risk Management Advisory Committee Members Present (Voting):

William Cooper, MD, MPH; Sonia Hernandez-Diaz, MD, DrPH; Karen Hopkins, MD (Consumer Representative); Peter Kaboli, MD; Elaine Morrato, DrPH; Jeanmarie Perrone, MD; Marjorie Shaw Phillips, MS, RPh, FASHP; Maria Suarez-Almazor, MD, PhD; T. Mark Woods, PharmD

Drug Safety and Risk Management Advisory Committee Members Not PresentPatrizia Cavazzoni, MD (Industry Representative); Brian Erstad, PharmD; David Madigan, PhD

Temporary Members (Voting):

Emilia Bagiella, PhD; Jan F. Chambers; Stephanie Crawford, PhD, MPH; Richard Denisco, MD, MPH; Angela Gravois (Patient Representative); Christopher Jones, PharmD, MPH; Winifred Landis, RPh, CDE, FAPhA; Karl Lorenz, MD, MSHS; Jane Maxwell, PhD; Rose May, CRNP; Laura McNicholas, MD, PhD; John Mendelson, MD; Melinda Moore PA-C; Lewis Nelson, MD; Mary Ellen Olbrisch, PhD, ABPP; Linda Simoni-Wastila, BSPharm, MSPH, PhD; Robert G. Smith, DPM, MSc, RPh, CPed; James H. Woods, PhD (Acting Chairperson); Michael Yesenko (Patient Representative); Robert W. Zaayer, PA-C

Acting Industry Representative to the Drug Safety and Risk Management Advisory Committee (Non-Voting):

Jose Vega, MD (Acting Industry Representative)

FDA Participants (Non-Voting):

Michael Klein, PhD; Bob Rappaport, MD; Judy Staffa, PhD, RPh; Douglas Throckmorton, MD

Speakers (Non-Voting, Presenting Only): Edward Michna, MD; Sharon Walsh, PhD

Guest Speakers (Non-Voting, Presenting Only): Eric Lavonas, MD; Kevin Zacharoff, MD, FACPE, FACIP, FAAP

Designated Federal Officer:

Kristina A. Toliver, Pharm.D.

Open Public Hearing Speakers:

Sen Joe Manchin, III (United States Senator); Rebecca Kirch (Director, Quality of Life and Survivorship, American Cancer Society); Kevin N. Nicholson, RPh, JD (Vice President, Government Affairs and Public Policy, National Association of Chain Drug Stores); Andrew Kolodny, MD (President, Physicians for Responsible Opioid Prescribing; Chair, Department of Psychiatry, Maimonides Medical Center); Cindy Steinberg (Chair, Policy Council, Massachusetts Pain Initiative; New England Regional Director, American Chronic Pain Association); Anita Ducca (Vice President, Regulatory Affairs, Healthcare Distribution Management Association); Lawrence Duda, DDS; Joe Mancini, MD; Steven Hayes; Shani Weber & Heather Pierce (Ehlers-Danlos National Foundation); Cheryl Placek; Patricia McDonald; Bob Twillman, PhD, FAPM (Director of Policy and Advocacy, American Academy of Pain Management); Lexi Reed Holtum (Vice President, The Steve Rummler Memorial Foundation); Judy Rumler (statement read by Lexi Holtum); Jerry Buechler; Sidney Wolfe, MD (Director, Health Research Group, Public Citizen); Ronna Hauser, PharmD (VP Policy and Regulatory Affairs, National Community Pharmacists Association); Elizabeth Terry (Policy Director, Long Term Care Pharmacy Alliance); Stephen A. Leedy, MD FAAHPM (Chair, Public Policy Committee, American Academy of Hospice and Palliative Medicine; Executive Vice President/Chief Medical Officer, Tidewell Hospice, Inc.); Avi Israel (President, Save the Michaels of the World).

The agenda was as follows:

Day 1: January 24, 2013:

Call to Order

Introduction of Committee

Introduction of Committee

Conflict of Interest Statement

Opening Remarks

<u>FDA Response to the Petition:</u> Controlled Substances Act Scheduling

Process

Overview of DEA's Request for Re-scheduling Hydrocodone

Combination Products from Schedule III to Schedule II of the Controlled

Substances Act (CSA)

<u>FDA Presentations continued – Office of Surveillance and Epidemiology (OSE):</u>

Drug Utilization Patterns for Combination Hydrocodone-Containing Products and Selected Opioid Analgesics Years 2007-2011

OSE Epidemiologic Analysis of Misuse/Abuse of Hydrocodone-containing Analgesics

Committee Questions to Presenters

Presentation by Speaker:

Abuse Potential of Hydrocodone in Human Studies

Committee Questions to Presenter

BREAK

James Woods, PhD

Acting Chairperson, DSaRM

Kristina A. Toliver, PharmD

Designated Federal Officer, DSaRM

Michael Klein, PhD

Director, Controlled Substance Staff (CSS)

Center for Drug Evaluation and Research (CDER), FDA

Julie Finegan, JD

Associate Chief Counsel for Drugs

Office of Chief Counsel

Office of the Commissioner, FDA

Silvia N. Calderon, PhD

Team Leader, Pharmacology Review Team

CSS, CDER, FDA

Rajdeep Gill, PharmD

Drug Utilization Data Analyst, Division of Epidemiology

(DEPI)-II

Office of Surveillance and Epidemiology (OSE), CDER,

FDA

Catherine Dormitzer, PhD, MPH

Epidemiologist, DEPI-II OSE, CDER, FDA

Sharon L. Walsh, PhD (Speaker)

Professor of Behavioral Science, Psychiatry and Director

of the Center on Drug and Alcohol Research

University of Kentucky

4

Presentation by Drug Enforcement Administration (DEA): FDA Drug Safety and Risk Management Joseph T. Rannazzisi **Advisory Committee** Deputy Assistant Administrator Concerning Hydrocodone Combination Office of Diversion Control U.S. Drug Enforcement Administration **Products** Committee Questions to Presenter LUNCH Presentation by Industry: Public Health Benefits and Risks of David Gaugh, RPh **Senior Vice President Sciences and Regulatory** Hydrocodone Combination Analgesic **GPhA Products** Affiliation/Generic Pharmaceutical Association (GPhA) Committee Questions to Presenter Presentation by Speakers: A Pain Physician's View of Impact of Edward Michna, MD, JD (Speaker) Schedule Change of Hydrocodone/APAP Director, Pain Trials Center Brigham and Women's Hospital Boston, Massachusetts Assistant Professor, Harvard Medical School Prescription Drug Monitoring Plans: Eric Lavonas, MD (Guest Speaker) **Evaluation of Effectiveness Associate Director** Rocky Mountain Poison and Drug Center Denver Health and Hospital Authority Associate Professor, Department of Emergency Medicine University of Colorado School of Medicine The Role of Education in Safe and Kevin L. Zacharoff, MD, FACPE, FACIP, FAAP Effective Pain Management (Guest Speaker) Vice President of Medical Affairs Inflexxion, Inc. **Committee Questions to Presenters BREAK**

Presentations by Professional

Associations:

Rescheduling Hydrocodone: Patient and

Public Health Considerations

American Academy of Pain Medicine (AAPM)

Lynn Webster, MD

President-Elect, AAPM Medical Director, CRI Lifetree

Salt Lake City, Utah

FDA Advisory Committee Hearing on

Potential

Rescheduling of Hydrocodone: Pharmacist and Pharmacy Issues to

Consider

American Pharmacists Association (APhA) Steve Simenson, BPharm, FAPhA, DPNAP

APhA President 2013-2014

President and Managing Partner, Goodrich Pharmacy,

Inc., Anoka, Minnesota

American Pharmacists Association (APhA)

Marcie Bough, PharmD

Senior Director, Government Affairs

APhA

American Dental Association & American Association of Oral and Maxillofacial Surgeons Hydrocodone Combination Analgesic

Frederick A. Curro, DMD, PhD

Products: Clinical Impact of a Schedule Director, PEARL Practice Based Research Network Change

Director Regulatory Affairs, Bluestone Center for Clinical

Research

Clinical Professor, Dept. of Oral Radiology, Pathology &

Medicine

New York University College of Dentistry

Drug Safety and Risk Management

Committee (DSaRM)

American Optometric Association

Jimmy D. Bartlett, OD

Chairman and CEO, Pharmakon Consulting Group

Health Benefits/Risks of Drugs

Containing Hydrocodone

American Society of Addiction Medicine

Phillip Bradley Hall, MD

WV Medical Professionals Health Pro

Executive Medical Director Bridgeport, West Virginia

Committee Questions to Presenters

ADJOURNMENT

Day 2- January 25, 2013:

Call to Order

Introduction of Committee

James Woods, PhD

Acting Chairperson, DSaRM

Conflict of Interest Statement

Kristina A. Toliver, PharmD

Designated Federal Officer, DSaRM

Summary of Day One

Acting Chairperson, DSaRM

James Woods, PhD

Open Public Hearing

BREAK

Open Public Hearing (cont.)

LUNCH

Presentation of Questions to the

Committee

James Woods, PhD

Acting Chairperson, DSaRM

Discussion/Vote by Committee

BREAK

Discussion/Vote by Committee (cont.)

ADJOURNMENT

Questions to the Committee:

Drug Safety and Risk Management Advisory Committee Questions:

1. (**DISCUSSION**) Please discuss what the pharmacology data and the epidemiology data suggest about the potential for abuse of hydrocodone combination products compared with drugs that are currently in schedule II.

Committee Discussion: Many committee members stated that the pharmacology data and the epidemiology data do not suggest that hydrocodone combination products have any less potential for abuse than other narcotic pain killers. Committee members stated that the non-narcotic additives do not lower the addiction potential of the combination products. However, they also noted that the epidemiology studies had deficiencies. The numerators used left many effects from addiction unknown. The denominators used led to contradictory results, thereby making the data unreliable, especially when looking at abuse ratios. Committee members also stated that dose is important to consider. Lower doses are considered to be less of a risk than schedule II drugs and that a great deal of the hydrocodone use is at the lower doses for acute pain. It was also noted that acetaminophen overdose is the leading cause of liver failure and liver transplant in the United States and that approximately one-half of those cases involve hydrocodone combination products. Please see the transcript for details of the committee discussion.

- 2. (**DISCUSSION**) Please discuss what impact rescheduling of hydrocodone combination products from schedule III to II would have on the following:
 - a. Prescribing patterns for opioids, including hydrocodone combination products. Committee Discussion: Committee members felt that overall there would be less prescribing of the hydrocodone combination drug products for medical use. Committee members expressed differing views on the details of the issue. Some felt that there will be an immediate impact and that prescribers will think twice about the number of pills they prescribe; thereby reducing the number of hydrocodone combination pills in circulation. Committee members stated concern that there will be a rollback in the scope of practice on certain prescribers, namely mid-level providers such as nurse practitioners and physician's assistants. There was also concern that this may lead to patients being abruptly withdrawn from hydrocodone combination products.
 - b. Delivery of healthcare in the US, including impacts on drug distribution, manufacturing, prescription and dispensing by pharmacies

 Committee Discussion: The committee stated that there will have to be a transition period before hydrocodone combination products are rescheduled. Otherwise there is a risk of loss of access to the drugs. During this transition period efforts should be made to educate prescribers and patients. Members were not concerned about the cost to the pharmaceutical industry. They were concerned about the impact rescheduling would have on healthcare outcomes.
 - c. Availability of hydrocodone combination products for patients with appropriate needs for them as well as by individuals seeking to abuse opioids.
 Committee Discussion: Many committee members stated that rescheduling hydrocodone combination products will increase the controls of the pills in the distribution system. However,

there was concern that many mid-level practitioners would no longer be able to prescribe hydrocodone combination products since physician's assistants can not write prescriptions for schedule II drugs in 15 states and nurse practitioners have the same restrictions in 9 states. This may lead to some patients not having access to hydrocodone combination products as access to physicians is limited. Similar concern was not expressed about the limitations on prescribing by

the optometrists who deliver healthcare services related to the eye to approximately half of the USA. Committee members stated that legislation may be needed to allow for mid-level practitioners to prescribe schedule II products. There was a suggestion to use the inconvenience that may result from rescheduling as a catalyst to address issues in the supply chain and with the prescribing process. There was also concern that heroin abuse would increase as a result of limiting access to hydrocodone combination products. Committee members cited the lack of population data about pain and the relationship of pain to opioid prescribing as hindering judgment with regard to likely public health effects with regard to pain.

d. Abuse and misuse of opioids, especially hydrocodone combination products.

Committee Discussion: Committee members stated efforts should be made to monitor current heroin abusers now as well as trying to prevent patients who would move from prescription opioids to heroin as a result of lack of access. Some committee members stated that rescheduling would decrease the potential for abuse; however other members felt that some people are genetically predisposed to abuse and nothing can be done about that. It was also suggested that some chronic pain patients may be better treated with other drugs.

Please see the transcript for details of the committee discussion.

3. (**DISCUSSION**) Please discuss whether there are other activities that could reduce abuse and misuse of these products?

Committee Discussion: Many members voiced support for prescriber and patient education, inter-state prescription drug monitoring programs including point of care applications, electronic prescribing for schedule II drugs, and long-term drug take back programs. There were calls for better, population-level data, rather than state-level data to better assess drug abuse and population level pain outcomes of policy. Members also suggested using risk-evaluation and mitigation strategies (REMS) to mitigate the risk associated with hydrocodone combination products. Members suggested working on primary prevention to reduce first exposures to hydrocodone combination products for purposes of abuse. Committee members also suggested partnering with the Department of Veterans Affairs, National Institutes of Health, Centers for Medicare and Medicaid Services, and other federal partners to address abuse. Opportunities include the institution of quality measures for pain and opioid prescribing, and regulatory efforts to assure that new electronic platforms (mobile and electronic health records) capture salient information about both prescribing practices and pain. Please see the transcript for details of the committee discussion.

4. **(VOTING)** Based on the background materials, presentations and the discussion above, do you recommend that hydrocodone combination products be rescheduled from schedule III to schedule II of the Controlled Substances Act (CSA)? Please explain the basis for your vote.

Yes: 19 No: 10 Abstain: 0 No Voting: 0

The committee members that voted yes stated that the pharmacology and epidemiology data shows no difference between the abusability of hydrocodone combination products and other schedule II products. They believed that current controls of these products are inadequate with regard to drug abuse; and that rescheduling is a first step in ushering in a new thought process, by prescribers and patients, about the use of hydrocodone combination products. Members also thought rescheduling would reduce the amount of drug product in circulation.

The committee members that voted no stated that rescheduling would result in an increased burden to patients and decreased patient access. Members were also concerned that limited access to hydrocodone combination products may lead to increased abuse of illicit drugs (such as heroin). There was concern

that increased prescribing of other schedule II products, which may have higher abuse potential, will be the net result of rescheduling. Committee members were also unsure whether or not rescheduling would address the abuse of hydrocodone combination products and that there is not sufficient data to support the rescheduling.

Please see the transcript for details of the committee discussion.

The meeting adjourned at approximately 4:15pm.